Fabrication of CMC/PVA/Dextrin-Based Polymeric Membrane for Controlled Release of Cefixime With Enhanced Antibacterial Activity

Arif Nazir[1] ⓘ, Mazhar Abbas[2], Dure Najaf Iqbal[1], Fadia Ameen[1], Samiah H. Al-Mijalli[3], Naveed Ahmad[4] ⓘ, and Munawar Iqbal[5] ⓘ

Abstract

This study focuses on the investigation of the significance of polymers in drug delivery approaches. The carboxymethyl cellulose (CMC), polyvinyl alcohol (PVA) and dextrin-based hydrogel membrane were prepared and employed for the sustained release of third-generation oral antibiotic (cefixime). Different proportions of CMC, PVA and dextrin were blended and hydrogel membranes were fabricated via solvent casting method. The prepared membrane was characterized by FTIR, SEM, UV-visible, TGA and swelling analysis. Cefixime drug was incorporated in the CMC/PVA/dextrin matrix and drug release was investigated. The sustained release of the tested drug (cefixime) was investigated and the drug was released in 120 min in the phosphate-buffered saline (PBS) solution. The antibacterial activity of the prepared membrane was promising against *Proteus vulgaris*, *salmonella typhi*, *Escherichia coli* and *Bacillus subtilis* strains. The swelling capabilities, thermal stability and non-toxic nature of the prepared CMC/PVA/dextrin membrane could have potential applications for cefixime drug in delivery in a controlled way for the treatment of infectious diseases.

Keywords

polymeric membranes, controlled drug release, antibacterial activity, cytotoxicity, cefixime

Introduction

In recent years, the development of advanced drug delivery systems has become imperative to optimize the therapeutic efficacy of pharmaceutical agents while minimizing potential side effects.[1,2] Controlled release systems, particularly polymeric membranes, have emerged as promising platforms for achieving sustained and targeted drug delivery.[3–6] Among the wide array of antimicrobial agents, cefixime, a third-generation oral cephalosporin, stands out for its potent antibacterial activity against a broad spectrum of gram-positive and gram-negative microorganisms. However, its short half-life and frequent dosing requirements necessitate the exploration of innovative drug delivery strategies to enhance its therapeutic effectiveness.[7–9] Cefixime exhibits good oral bioavailability (around 40-50%), and controlled release systems can further enhance its absorption and protect the drug

[1] Department of Chemistry, The University of Lahore, Lahore, Pakistan
[2] Department of Basic Science (Section Biochemistry), University of Veterinary and Animals Science Lahore, Jhang, Pakistan
[3] Department of Biology, College of Sciences, Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia
[4] Department of Chemistry, Division of Science and Technology, University of Education, Lahore, Pakistan
[5] School of Chemistry, University of the Punjab, Lahore, Pakistan

Corresponding Authors:
Arif Nazir, Department of Chemistry, The University of Lahore, Lahore 54000, Pakistan.
Email: anmalik77@gmail.com

Samiah H. Al-Mijalli, Department of Biology, College of Sciences, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia.
Email: shalmejale@pnu.edu.sa

from enzymatic degradation.[10] It has a moderate half-life (around 3-4 hours), making it suitable for controlled release systems aiming for extended drug release over 6-12 hours.[11,12] Its solubility in water facilitates its incorporation into various dosage forms and release mechanisms. Various controlled release technologies can be employed, including polymers,[13,14] matrices, microspheres, liposomes etc. depending on the desired release profile and the target site. Cefixime's pharmacokinetic, stability, therapeutic, and design-friendly properties make it a promising candidate for controlled drug delivery systems.[15,16] Careful consideration of its properties and potential challenges can guide the development of effective and patient-centric interventions.[17,18]

To overcome these challenges, the present research introduces a novel polymeric membrane composed of carboxymethyl cellulose (CMC), polyvinyl alcohol (PVA), and dextrin for the controlled release of cefixime. This tricomponent system consists of three unique molecules that work together to improve the drug-delivery capabilities of the membrane. Carboxymethyl cellulose[19–21] is used for supporting the membrane's structural integrity and enabling long-term drug release. Polyvinyl alcohol[22] is well-known for its film-forming and biocompatibility qualities.[23] Because of its high mechanical strength and hydrophilic character, polyvinyl alcohol works well with CMC to limit drug diffusion and improve membrane stability.[24,25] The combination of CMC, PVA, and dextrin for film preparation offers a synergistic approach to address various challenges in controlled drug delivery. CMC contributes to film-forming ability and biocompatibility, while PVA enhances mechanical stability and mucoadhesive properties. Dextrin acts as a plasticizer, improving flexibility and drug release kinetics. Together, these polymers provide films with enhanced adhesive qualities, regulated drug release, and desirable mechanical characteristics. This polymer combination plays a crucial role in maintaining sustained release profiles of drugs like cefixime, ensuring prolonged therapeutic levels in the body.[26,27] Enhanced adhesion improves drug retention at the application site, facilitating longer contact and absorption, while controlled release kinetics maximize antibacterial activity against pathogens and minimize side effects. The selection of polymers also affects the stability and solubility of the drug in the film matrix, further influencing its antibacterial efficacy and release profile. Overall, the blend of CMC, PVA, and dextrin offers a balanced solution to overcome individual polymer limitations and achieve controlled drug release with improved therapeutic outcomes.[28–30]

To address delayed diabetic wound healing, a novel multifunctional hydrogel was developed, incorporating carboxymethyl chitosan, 2,3,4-trihydroxybenzaldehyde, copper chloride, and graphene oxide-N, N'-di-sec-butyl-N, N'-dinitroso-1,4-phenylenediamine (GO-BNN6). This hydrogel demonstrated stability, self-healing, conductivity, antioxidant, and antibacterial properties.[31] An enhanced biodegradability is promoted by the water-soluble carbohydrate derivative

dextrin, which also modifies drug release kinetics.[25,32] This recent study introduces self-adaptive wound dressings by incorporating MoS_2-loaded nanozyme into pH, NIR, and temperature-responsive cryogels. The cryogels exhibit acid-triggered bacterial capture capacity and enhance photodynamic antibacterial efficiency. They enable controllable on-demand delivery of reactive oxygen species (ROS) and nitric oxide (NO), effectively eliminating MRSA biofilm through NO-assisted photodynamic and photo-thermal therapy. These multi-stimuli-responsive cryogels reduce wound infection, alleviate oxidative stress, and accelerate healing processes, offering a promising solution for infected wound treatment.[17] This research aims to create a flexible and effective drug delivery system by combining polymers into a single membrane. Glutaraldehyde is added to form a three-dimensional network within the polymer matrix, enhancing mechanical strength and durability. Controlled release of cefixime from this matrix is expected to prolong therapeutic benefits, reduce dosing frequency, and minimize side effects due to consistent drug concentrations. The membrane is also anticipated to exhibit increased antibacterial activity, ensuring optimal medication levels at infection sites for an extended duration.

Based on the aforementioned facts, this research represents a significant step forward in the design and fabrication of polymeric membranes for drug delivery applications. The synergy between CMC, PVA, and dextrin, coupled with the controlled release of cefixime, holds the potential to revolutionize the treatment of bacterial infections by providing a more efficient and patient-friendly therapeutic approach. Glutaraldehyde acts as a crosslinking agent that forms covalent bonds between the polymer chains of CMC, PVA, and dextrin. The fabrication process, characterization and the CMC/PVA/dextrin-based polymeric membrane for controlled release of cefixime were investigated.

Materials and Methods

Chemicals and Reagents

Polyvinyl alcohol (PVA) (Mw ∼ 30,000-70,000; viscosity. *4-6 cP, 4% in* H_2O (20°C), carboxymethyl cellulose (Mw ∼ 700,000) were purchased from Sigma Aldrich. All other materials were procured from the specified named supplier. Dextrin from corn starch (Mw ∼ 504.438) from Fisher Scientific, *Glutaraldehyde*, 50% solution; (Mw ∼ 100.12) from Junsei Chemical Co., Ltd. Sodium hydroxide and sulfuric acid were purchased from Sigma-Aldrich. Deionized water was used for the preparation of the aqueous solutions.

Preparation of Membranes without Drug Loading

The CMC, PVA, and dextrin was dissolved in deionized water using a magnetic stirrer at gentle heat (around 40-50°C) until a clear solution was formed, which was cooled down and glutaraldehyde solution was added dropwise with continuous

stirring for 15-30 min. The neutral condition (pH ∼ 7) was maintained using a buffer solution. The cross-linking reaction proceeded until the hydrogel formed, cured at an elevated temperature and poured the solution into the petri plate. A gel of uniform thickness was formed at room temperature in 24-48 h. To remove residual glutaraldehyde, the gels were immersed in deionized water for several days by changing after every 12 h. Before storing and further processing, gels were gently dried in a vacuum at 40°C. The concentration of CMC in hydrogels for drug delivery typically ranges from 1 to 5% (w/v), PVA .5 to 2% (w/v), dextrin .5 to 1% (w/v), glutaraldehyde .1 to .5% (v/v). Similarly, sample codes (CPDG#2-5) are fabricated by varying the concentrations of polymer, while keeping the quantity of cross-linker glutaraldehyde constant. The sample compositions are listed in Table 1. Finally, the hydrogel was washed to remove any residual reactants, unreacted polymers, or any other by-products. After washing, the hydrogel it was dried at room temperature.[33]

Preparation of Membranes with Drug Loading

The drug is loaded in CPDG#2 with the same composition of CMC, PVA, and dextrin, as mentioned above. Dextrin solution was prepared by the addition of 3 g of dextrin in 30 mL distilled water with constant stirring and heated at 70°C for an hour then cefixime drug (10 mg) was added onto this solution of dextrin. When the drug was dissolved in the dextrin solution the prepared solution of dextrin was added to CMC, PVA solution, which was also prepared as the procedure was adopted for CPDG#1 fabrication. Cross-linker (GA) .1 mL was also added to this solution and continuous stirring was done at 70°C for 5 h (Figure 1). Then, poured the mixture in a Petri plate and dried for 24 hours at 40°C. The membranes containing 25 mg and 50 mg drugs were also prepared by the same procedure, which was named CPDG#3 and CPDG#4.[34]

Characterization Techniques

Hydrogel characterization was performed by FTIR, UV-visible, TGA and SEM techniques. The prepared hydrogels were also studied for their antibacterial activity and cytotoxicity analysis. FTIR spectroscopy was used for detecting the functional groups in a blended membrane as well as probable molecular interactions among chemical compounds in the membrane. FTIR analysis of membrane was carried out

using a Bruker Alpha-II spectrometer through a resolution of $16\ cm^{-1}$ in a wavenumber range from 500-4000 cm^{-1}. A UV-Vis spectrophotometer was used to check the absorbance of supernatant solutions and aliquots (Shimadzu, model: UV-1800). Using the Beer-Lambert law ($A = \varepsilon CL$), the technique is commonly employed in quantitative analysis to calculate the concentration of an absorbing species in solution.[35] TGA is a thermal analysis method that measures the mass of a sample through time as the temperature varies. Using TGA, we analyzed the membrane which was carried out by Thermogravimetric Analyzer TGA Q50 V20.10 Build 36 Model under a nitrogen environment, a TGA Heat Exchanger system with a heating rate is about 10 °C/min was used. TGA is a valuable method for assessing the heat stability of materials polymers.[36] The SEM is one of the techniques to analyze the surface morphology of the material. SEM analysis was employed to evaluate the morphology.[37] A Zeiss SEM-type Ultra-Plus scanning electron microscope was utilized to analyze the morphology of the hydrogel membrane.

Drug Release Analysis

The rate of drug release would be proportional to the hydrogels' equilibrium swelling ratio. Immersing 50 mg drug-loaded hydrogel membrane in 100 mL phosphate buffer solution of pH ∼ 7.4 was kept at 37°C, which was shaken for regular intervals and used for in vitro drug release investigation as a function of time. A 5 mL of solution was withdrawn and absorbance was measured at 293 nm at regular time intervals. The volume was maintained by replacing the buffer solution (3 mL) each time.

Antibacterial Activity

Using a nutrient agar medium, a pure culture of bacterial strains was established. For this investigation, 1.2×10^8 CFU/mL inoculum of all identified microorganisms was utilized. In 1 mL sterilized distilled water, 10 mg membranes (CPDG#1, CPDG#2) were dissolved. 20 mL of sterilized nutrient agar was added as well as 100 μL of fresh bacterial culture with each sterilized disposable petri plate, mixed well, or set aside for solidification over 20 min at room temperature. The wells were induced in each Petri plate using a sterilized process, and then 100 μL containing membrane sample and control

Table 1. Detail of Membranes Sample Preparation Without Drug Loading.

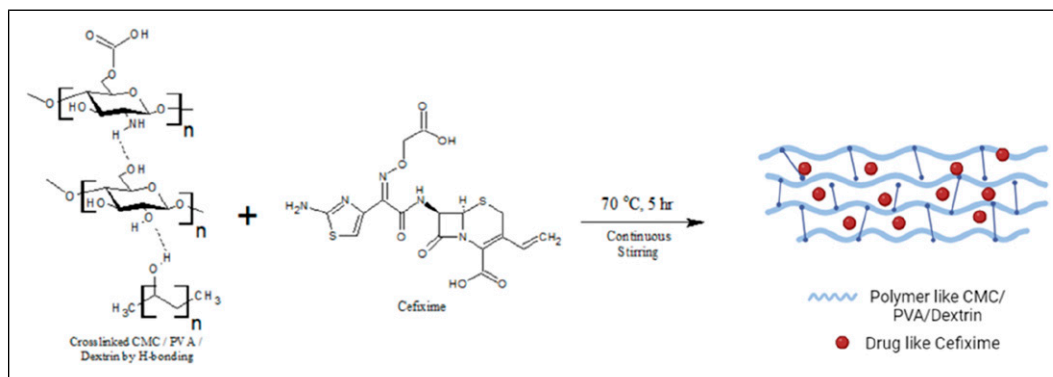| Sr. #	Sample Code	CMC (%) w/v	PVA (%) w/v	Dextrin (%) w/v	GA (Cross linker) (v/v)
1	CPDG#1	1	0.5	0.5	0.1 (mL)
2	CPDG#2	2	0.4	0.4	
3	CPDG#3	3	0.3	0.3	
4	CPDG#4	4	0.2	0.2	
5	CPDG#5	5	0.1	0.1	

Figure 1. Schematic for the fabrication of CMC/PVA/dextrin-based polymeric membrane for Controlled release of cefixime.

(ciprofloxacin 1 mg/mL) were poured into each well. After 10 min, petri plates were transferred into incubate at 37°C for 24 h for bacteria growth and sample showing their antibacterial potential, clear zone was recorded using a zone reader in reported in millimeter (mm).

Biodegradation Study

In vitro biodegradation of hydrogel samples (50 mg) was evaluated by immersing them in phosphate-buffered saline (PBS) solution. The amount of weight lost was observed for each formulation for different time intervals. At every time interval, the hydrogel samples were taken out of the PBS solution, and weight loss was noted. The weight loss that was seen over time was indicative of the hydrogels' biodegradation process. This approach enabled the evaluation of the in vitro biodegradation behavior of the hydrogels, which is useful for its biomedical applications.

Cytotoxicity Analysis by Hemolytic Assay

The cytotoxicity studies of the hydrogel loaded with cefixime was analyzed by hemolytic assay, a method with some modification.[38] Three mL of freshly obtained bovine blood was added in heparinized tubes to avoid coagulation and gently mixed, poured into a sterile 15 mL falcon tube and centrifuged for 5 min at 850 × g. The supernatant was poured off and RBCs were washed three times with 5 mL of chilled (4°C) sterile isotonic phosphate buffer saline (PBS) solution, adjusted to pH ∼ 7.4. The washed RBCs were suspended in the 20 mL chilled PBS. Erythrocytes were counted using a hematology analyzer and RBC count (4.068 ×10^6/μL) was used for this study. After dissolving 10 mg of the membrane (CFX 50, CPDG#2) into 1 mL water, 50 μL of the stock solution of (CPDG#1, CPDG#2) was mixed with 180 μL of red blood cell (4.068 ×10^6/μL). The reaction samples were incubated at 37°C for 30 min with continuous agitation. After the incubation was finished, the tubes were quickly cooled on ice for 5 min and then centrifuged for 5 min at 1310 × g. The

supernatant, 100 μL was collected and diluted with 900 μL of phosphate buffer saline (PBS), the whole process was done under a control condition to minimize the cell lysis from external factors. After that, a 200 μL sample was poured into 96 well plates along with a negative control of phosphate buffer saline and a positive control of .1% Triton x-100. Using a micro-plate reader absorbance was recorded at 576 nm (BioTek, Winooski, VT, USA). The percentage of cell lysis was recorded using the relation shown in equation (1).

$$\text{Lysis of RBCs}\,(\%) = \frac{\text{Absorbance of sample}}{\text{Absorbance of Triton}\,(X-100)} \times 100 \tag{1}$$

Results and Discussion

Properties of the Membranes

The material's functional groups are identified using Fourier transform infrared spectroscopy. FTIR analysis of CMC/PVA/dextrin hydrogel membranes was recorded at room temperature in 500-4000 cm^{-1} and results are shown in Figure 2. The IR spectra of pure PVA have three main regions. The first region is broad and the strong absorption band appears at 3266.62 cm^{-1} which is linked to the hydroxyl group stretching O-H. The next region displays the slightly strong bonding at the wavelength of 2859-2882 cm^{-1}. In the pure PVA structure, the peak that appeared in this region is of C-H stretching. The third region, which is related to C–O stretching, exhibits weak bonding and is revealed at 1050-1500 cm^{-1} range.[39]

The IR spectra of CMC indicate the stretching peaks including a broad peak for O-H stretching at 3230 cm^{-1}, C-H stretching at 2891 cm^{-1}, 1588 cm^{-1} peak due to C = O stretching and C-O stretching at 1016 cm^{-1} was observed.[40] The IR spectra of dextrin were found in the 3860-3230 cm^{-1} range, which refers to the O–H bond and the band at 2928 cm^{-1} indicates the vibration of the C–H bond. The band detected at 1540-1430 cm^{-1} is due to H-O-H bending
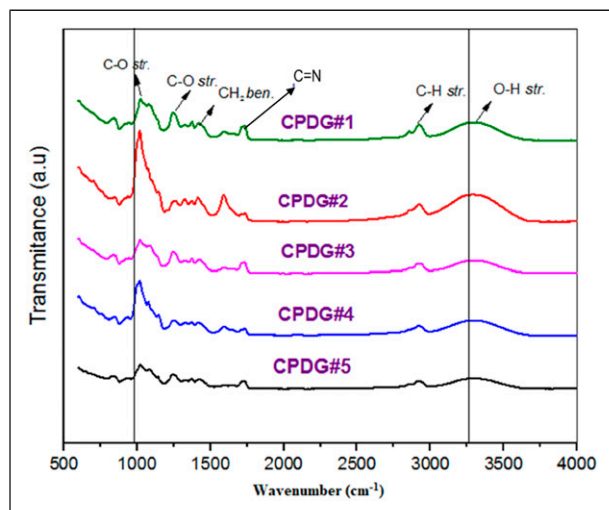
Figure 2. FTIR spectra of synthesized hydrogel membranes (CMC, PVA and dextrin).

vibration. The bands for C-O and C-O-C groups appear at 1160 and 1028 cm^{-1}.[39]

The IR spectra of CPDG#1 revealed the peak, which indicates the presence of interaction between PVA, CMC and dextrin. The broad and strong absorption band of O-H stretching appeared at 3293.46 cm^{-1} and for C-H stretching from the alkyl group, the peak was observed at 2918.75 cm^{-1}. The carbonyl (C = O) peak intensity was decreased as the PVA content was increased. This demonstrates that when the concentration of PVA increased, cross-linking decreased.[26] At the wavelength range of 1242.05 cm^{-1} C-O stretching of acid (carboxylic acid) and C-O stretching also appeared at 1020.70 cm^{-1}. Characteristics peak due to CH$_2$ bending at 1417.68 cm^{-1}, C-O-C stretching vibrational peak at 1078.80 cm^{-1} was also detected.

Similarly, the IR spectra of CPDG#2-5 explained the distinctive absorption bands of O-H stretching at 3284.06-3292.86 cm^{-1}. The C-H stretching of the alkyl group was observed at 2921.95-2923.46 cm^{-1} and the C = O stretching due to the aldehydic group furnished the peak between 1591.19-1594.94 cm^{-1}. The C-O stretching of acid (carboxylic acid) at 1243.80-1257.03 cm^{-1}, C-O-C stretching vibrational peak was observed only in samples CPDG# 1 and 2 at 1078.80 and 1077.00 cm^{-1}. The peak of CH$_2$ bending was appeared at 1372.22-1420.05 cm^{-1}. A new peak that appeared between 1640 cm^{-1} and 1655 cm^{-1} indicated that the crosslinking process was successful and that imine bonds had formed between the hydroxyl groups of the polymers and glutaraldehyde. The degree of crosslinking was qualitatively determined by comparing the relative strength of this imine bond peak to the residual C = O peak from unreacted glutaraldehyde. In addition, variations in the intensity and orientation of pre-existing peaks, specifically in the vicinity of 1000-1200 cm^{-1} (C–O stretching) and 1600-1800 cm^{-1} (C = O stretching) offered interactions and modification within the

hydrogel network. Absorption values of all the membranes CPDG#1 to CPDG#5 are given in Table 2. UV-Vis spectra were recorded (Shimadzu 1800 model) UV-Vis spectrophotometer in the wavelength range of 200-800 nm and Figure 3 depicted the UV-Vis absorption spectra of the synthesized membrane.
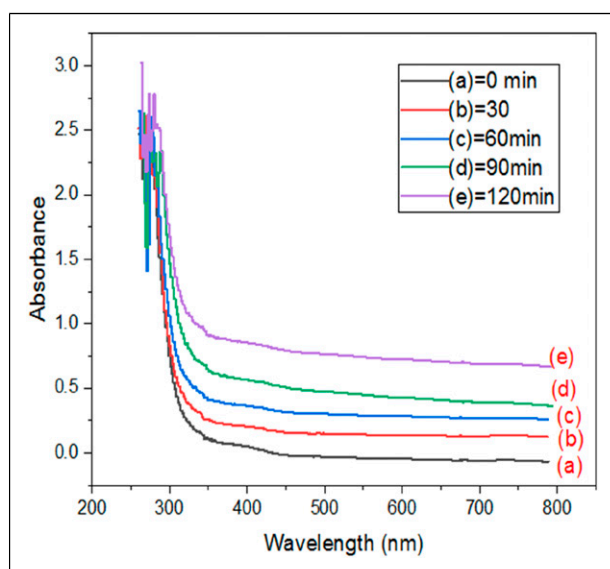
Thermogravimetric Analysis

Thermal gravimetric analysis (TGA) spectra generally exhibit three discernible phases of weight loss in carboxymethyl cellulose (CMC) and polyvinyl alcohol (PVA). The initial phase, which corresponds to the evaporation of moisture absorbed by the samples, takes place at relatively moderate temperatures, reaching 200°C for CMC and 150°C for PVA. During this phase, volatile components may also be lost in the case of CMC. The primary decomposition process occurs during the second stage, which occurs at elevated temperatures (150-450°C for CMC and 300-450°C for PVA). The polymer chains degrade during this phase, liberating gaseous byproducts including carbon dioxide and water vapour. Several variables affect the specific temperature range and decomposition rate, including the degree of hydrolysis for PVA and the heating rate and other unique properties of the polymer. Ultimately, exceedingly high temperatures result in the formation of a plateau, which symbolizes the remaining mass of non-volatile constituents that persist after decomposition. The residual weight of the polymers offers valuable information regarding their thermal stability and purity (Fig. S1).

The TGA curves are shown in Figure 4 which differentiates the loaded and the unloaded membrane. The weight loss phases of the hydrogels can be observed by thermograms. Firstly, both membranes showed evaporation of the moisture content followed by weight loss at 200°C due to readily degradable components like glycerol.[41] The TGA curve of the CPDG#2 unloaded membrane indicated two main weight losses. The first weight loss indicates the weight loss appeared between 250 and 400°C because of the breaking in polymer chain linkages like hydrogen bonding in both polymers (PVA and CMC). Thermal degradation or depolymerization of both PVA as well as CMC, and also dehydration for CMC saccharide rings. The second indication of weight loss was observed at temperatures between 400 and 550°C, which may be linked to the formation of PVA and CMC as byproducts of the thermal breakdown process.[42]

In the case of drug-loaded membrane, the TGA curve of polymer blends revealed a small weight loss at 60-150°C, which is due to water molecule evaporation, the second (150-200°C) phase was attributed to polymer degradation and at third phase (200-250°C), the degradation was due to polymeric chain. Thermal stability was slightly low due to a change in crystallinity of the membrane and thermal stability was observed at 400°C.[43] Furthermore, thermograms of both loaded and unloaded hydrogels indicated that the presence of

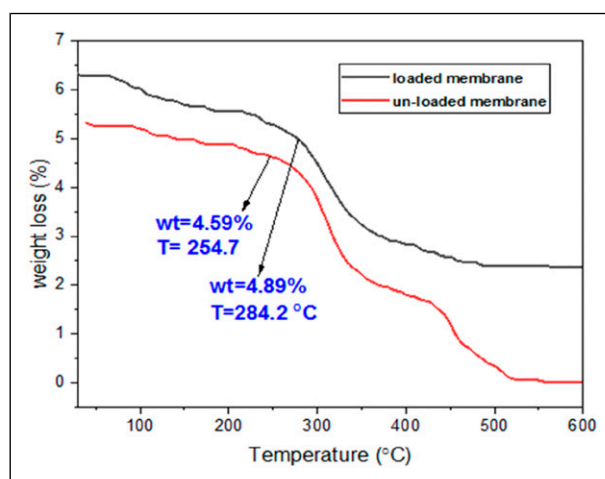**Table 2.** Absorption Values of the Blended Membrane in FTIR Spectra.

Functional Group	CPDG#1 (cm^{-1})	CPDG#2 (cm^{-1})	CPDG#3 (cm^{-1})	CPDG#4 (cm^{-1})	CPDG#5 (cm^{-1})
O-H *str.*	3293.46	3284.06	3292.25	3284.29	3292.86
C-H *str.*	2918.75	2923.46	2921.95	2923.37	2922.21
C = O *str.* In aldehyde	—	1591.81	1594.94	1591.19	1593.29
C-O *str.* Carboxylic acid	1242.05	1248.61	1243.80	1257.03	1244.18
C-O *str.*	1020.70	1016.44	1021.99	1018.49	1020.03
CH$_2$ *ben.*	1417.68	1372.22	1419.12	1414.90	1420.05
C-O-C *str.* Vibration	1078.80	1077.00	—	—	—
Imine bond C = N	—	1640-1655	1640-1655	1640-1655	1640-1655

Figure 3. UV-vis absorption spectra hydrogel membranes (PVA, CMC, dextrin).

Figure 4. TGA analysis (A) unloaded membrane PVA, CMC and dextrin (B) cefixime drug loaded membrane of PVA, CMC and dextrin.

the drug-loading membrane enhances thermal stability. This enhancement suggests a stronger interconnection between the polymers, possibly due to crosslinking, which contributes to the improved thermal stability observed.

Surface Morphology

The hydrogel surface is one of the essential factors influencing drug release behavior.[42] SEM analysis was used to analyze the surface morphology of the prepared membranes.[37] The SEM images of drug-loaded and unloaded hydrogel membranes were obtained and compared (Figures 5 and 6). The loaded and unloaded hydrogels revealed a significant change in surface morphology. The unloaded hydrogel membrane has a smooth surface which indicates excellent polymer blending and the loaded hydrogel membrane showed cracks and a spherical shape inside the matrix. The results also revealed that the formation of spherical structures indicated the cefixime drug in the loaded

membrane, which is useful for its application in drug delivery[39] and water molecules may absorb easily because of the hydrogel network's interconnected cracks, affecting the rate of drug release. These cracks are also predicted to be water permeation zones and external stimuli interaction sites, such as temperature, pH ionic strength etc.

Biodegradation Study

The results of a biodegradation experiment on the prepared hydrogels submerged in PBS solution are shown in Figure 7. On days 1, 3, and 6, the CPDG#2 sample showed weight reductions of 35.5%, 26.3%, and 16.2%, respectively. The CPDG#3 samples showed similar biodegradation patterns, although CPDG#3 biodegradation was slightly lower than the CPDG#2 samples. These results suggest that there may be differences in the crosslinking density or structural makeup of the hydrogel formulations, which could influence how easily they break down chemically or enzymatically in PBS. The distinct hydrogel formulations' differing biodegradation rates highlight how formulation parameters affect degradation
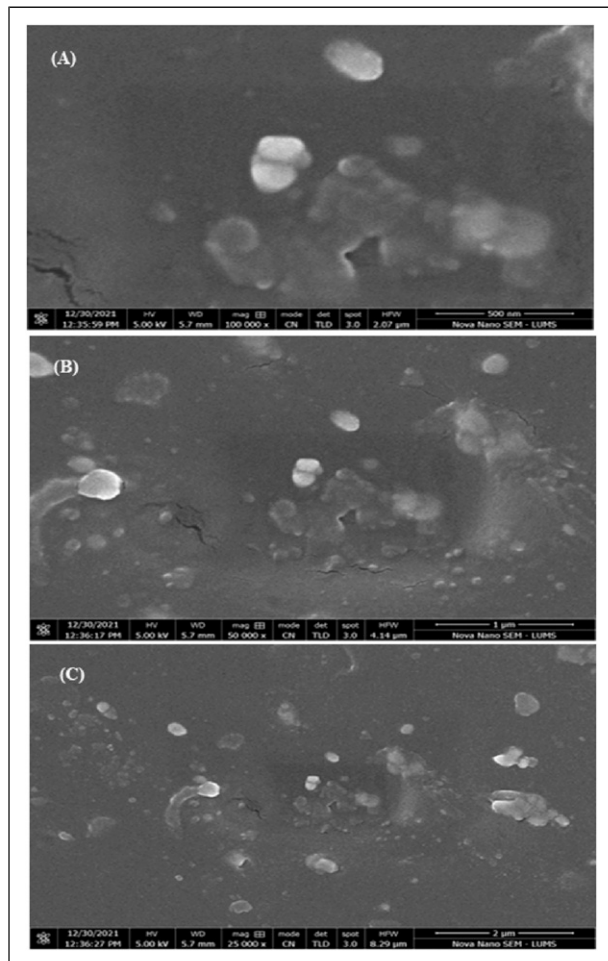
Figure 5. Surface morphology hydrogel membrane without drug loading at different magnifications, (A) 100Kx, (B) 50Kx and (C) 25Kx.

Figure 6. Surface morphology of drug-loaded hydrogel membrane at different magnifications, (A) 100Kx, (B) 50Kx and (C) 25Kx.

behavior. These revelations provide important details regarding the hydrogels' biodegradation kinetics. Hydrogel formulations customized for particular biomedical applications may be made easier with more research into the fundamental mechanisms causing these variations in biodegradation rates. The biodegradation of hydrogels based on CMC/PVA/dextrin can be influenced by various factors. The hydrogel's composition, specifically the ratios of PVA, CMC and dextrin, can affect how susceptible it is to biodegradation. Differentiating degradation rates may also be caused by the polymers' chemical makeup and susceptibility to the medium. The degree of crosslinking affects the hydrogel network's stability and resistance to breaking down. Slower rates of biodegradation are generally the result of higher crosslinking densities, which also improve network stability.[17] In addition, the hydrogel's physical properties, like pore size and distribution, can influence the biodegradation mode. Larger pore sizes and increased interconnectivity could enhance the degradation by making it easier for degrading agents to enter polymer chains.[27]
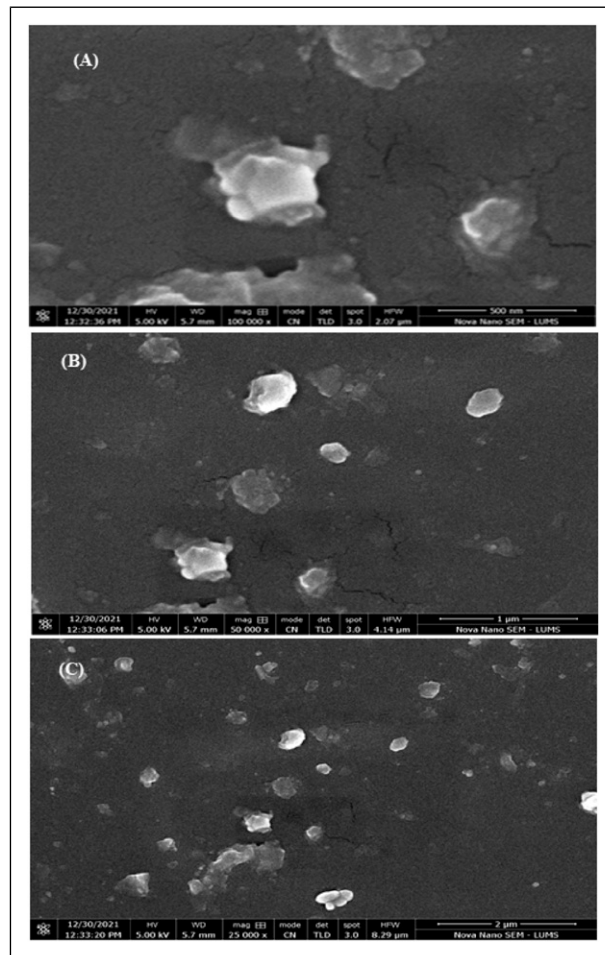
Drug Release Analysis

The drug-loaded membranes, CPDG#2 and CPDG#3 were submerged in a solution of 100 mL phosphate-buffered saline (PBS) at pH $\sim$ 7.4 and kept at 37°C to examine the drug's release behavior (Figure 8). The drug release was monitored for 120 min and in the case of CPDG#2, the drug release (10.8%) was started within the first 10 min and increased linearly over the next 60 min, reaching 98.15% at the end of 120 min. Comparably, for CPDG#3, the drug release was observed to be 14.2% during the first 20 min and to increase over the next 110 min, reaching 90.6%. According to the analysis of the data, the rate of drug release was first rapid and then gradually decreased over time. It is possible to deduce from the results that the CMC/PVA/dextrin membrane has the potential to deliver drugs depending on pH. Stimuli-responsive hydrogels can react to outside stimuli, like variations in temperature, exposure to light, or changes in pH.[29] These stimuli are useful for controlling and enabling on-demand release mechanisms by modulating drug release rates.[26] The prepared membranes that are stimuli-responsive
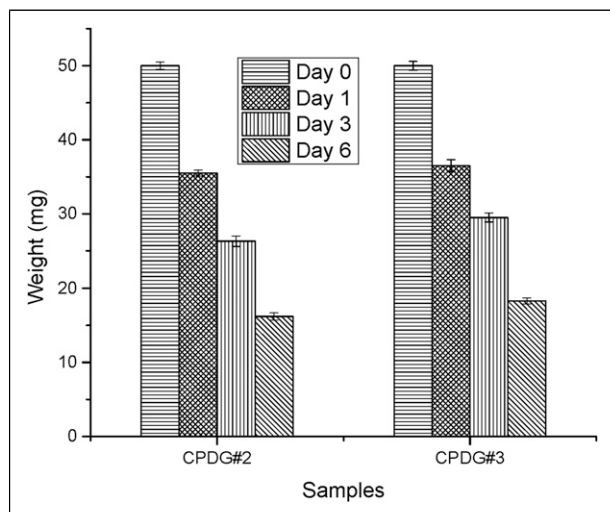
Figure 7. Biodegradation behavior of hydrogel membranes in Phosphate-buffered saline.

Figure 8. The drug release percentage from the drug-loaded hydrogels as a function of time.

can react to outside stimuli, like variations in temperature, exposure to light, or changes in pH. These stimuli are useful for controlling and enabling on-demand release mechanisms by modulating drug release rates.[28] The release mechanism of cefixime from the CMC/PVA/dextrin membrane involves several factors. Upon exposure to aqueous environments, the membrane matrix swells, allowing water molecules to penetrate and interact with the polymer network, thereby creating pathways for drug diffusion. Concentration gradients drive the diffusion of cefixime molecules through the swollen membrane. Various factors, including the size and charge of the drug molecules, as well as the porosity and mesh size of the membrane matrix, influence the rate of diffusion.[27,30] Additionally, the integrity of the membrane may degrade over time due to hydrolysis or enzymatic breakdown, potentially leading to the release of encapsulated drug molecules.[26,44]

Antibacterial Activity

Using the well diffusion method, the antibacterial activity of (CPDG#1, CPDG#2) was evaluated against a panel of microorganisms (*Proteus vulgaris*, *salmonella typhi*, *Escherichia coli* and *Bacillus subtilis*) are shown in Figure 9. Antibacterial activity of the sample reduced bacterial load in culture medium and resulting clean zones recorded using zone reader and results of growth inhibition potential of cefixime loaded in hydrogel was measure in mm.[45] Using the disc diffusion method, the antibacterial activity of membranes against gram-positive and gram-negative bacteria was determined and given in Table 3. For centuries ago, various infectious diseases caused by different pathogenic bacteria have been a main anxiety to the progress and existence of humans. These diseases are a global burden and the leading cause of death around the world. Hydrogel-based drug delivery
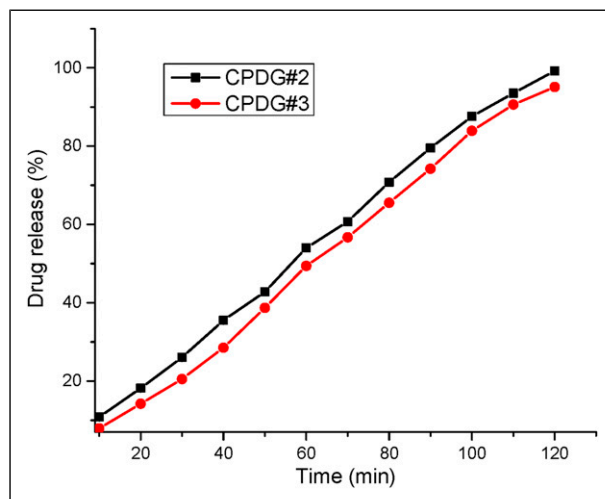
systems have emerged as the most effective strategy for eradicating various bacterial infectious diseases.[31] The best antibacterial activity of the PVA/CMC/dextrin in hydrogel films could be explained by the efficient release of cefixime in the medium. It was concluded that gram-negative bacteria *E. coli* showed the best antibacterial activity with synthesized hydrogel films.

Cytotoxicity Studies

Red blood cells (RBCs) were used to examine the cell lysis against the prepared drug-loaded hydrogel membranes. Table 4 displays the RBC lysis activity of the drug-loaded membrane, CPDG#1 was $4.20 \pm 2.27\%$ of cell lysis and CPDG#2 revealed a cell lysis of $5.32 \pm 3.43\%$. The drug cytotoxicity analysis is an important parameter in drug development. Previous studies reported that the hydrogels carboxymethyl cellulose (CMC) demonstrated poor mechanical strength and are superabsorbent, but other constituents of hydrogels can increase mechanical strength while reducing drug loading capacity and swelling. To test their inherent swelling capacities and mechanical strength, the hydrogels were produced by crosslinking β-cyclodextrin (βCD) or carboxymethyl-β-cyclodextrin (cmβCD) with CMC and cellulose. The cmβCD/CMC hydrogels exhibited the greatest antibacterial activity of all the hydrogels tested. The hydrogels cmβCD/CMC were not cytotoxic to human skin fibroblasts, signifying that they are appropriate to apply as an effective, bio-friendly, and non-toxic drug delivery vehicle.[46] Also,[47] prepared the novel biopolymer-based graphene oxide (GO) loaded cross-linked Na-alginate hydrogels, which were subsequently characterized using various statistical methods. It showed that the thermal strength of the hydrogel rises with the loading of GO. The swelling ability of the hydrogels indicated
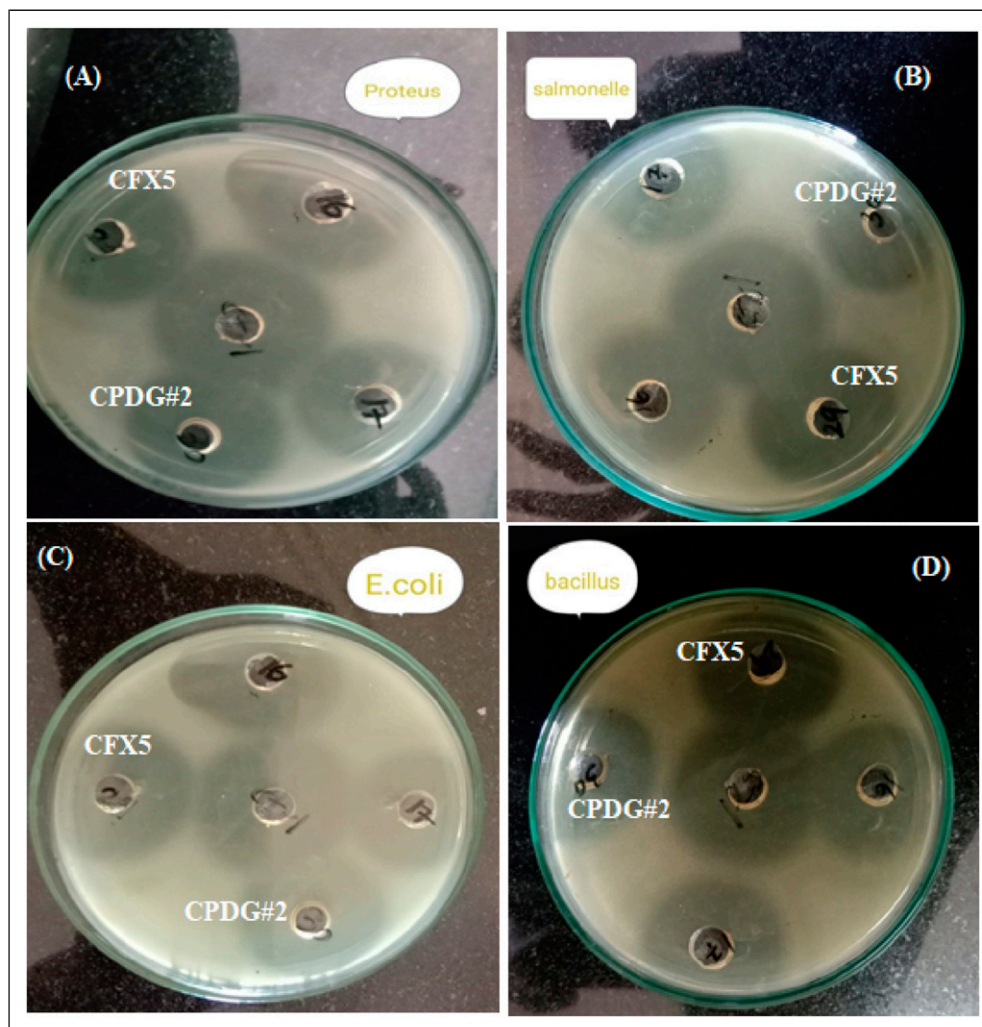
Figure 9. Antibacterial activity (zone of inhibition in mm) of PVA, CMC, dextrin and cefixime membrane against (A) *Proteus vulgaris* (B) *Salmonella typhi* (C) *Escherichia coli* and (D) *Bacillus subtilis*.

Table 3. Antibacterial Activity of the Membrane Against Gram-Positive and Gram-Negative Bacterial Strains.

Sample Code	*P. vulgaris*	*S. typhi*	*E. coli*	*B. subtilis*
CPDG#2	18 ± 1.30	19 ± 2.80	21.57 ± 2.10	22.3 ± 1.50
CPDG#1	12 ± 1.50	13.2 ± 2.40	14.6 ± 2.40	14.3 ± 2.60
Ciprofloxacin	28.5 ± 1.20	29.3 ± .80	28 ± 1.20	29.67 ± 1.10

Bacterial name: *P. vulgaris*: Proteus vulgaris, *S. typhi*: Salmonella typhi: *E. coli*: Escherichia coli: and *B. subtilis*: Bacillus subtilis. The values are mean ± SD of triplicate samples (n = 3); the standard drug Ciprofloxin (1 mg/mL).

that neutral solutions swell the most, whereas basic and acidic solutions swell similarly. Similarly,[48] studied that the use of wound dressings exhibiting antibacterial activity, non-toxicity, or excellent mechanical qualities to treat infections has garnered a lot of attention. Silver nanoparticles were encased in hydrogels made of carboxymethyl starch, polyvinyl alcohol, and citric acid (CMS/PVA/CA). These hydrogels containing Ag NPs-50 had the lowest inhibitory concentration against *E. coli* and *S. aureus*.

The Na-CMC/PVA microsphere has been prepared using water in an oil emulsion crosslinking process.[49] The use of chitosan to encapsulate Na-CMC/PVA microspheres was successful in slowing FBP release in the gastro-stomach area. The coating was further corroborated by SEM pictures, which revealed the smooth surfaces of the drug-loading coated microspheres. It was revealed that the coating approach is particularly useful for extending the release of pharmaceuticals with a short plasma half-life, increasing drug loading, and

Table 4. In-vitro cytotoxicity (%) Against Red Blood Cells (RBCs).

Sr.#	Sample Code	Cytotoxicity (%) against RBCs
1	CPDG#1	4.20 ± 2.27
2	CPDG#2	5.32 ± 3.43
3	Phosphate buffer saline (Negative control)	1.20 ± 1.23%
4	Triton-x100 (.1%) (Positive control)	100%

A sterile chilled buffer, Phosphate buffer saline (pH ~ 7.4) was used as the negative control (0% background RBCs cell lysis) and Triton x-100 (.1%) was used as a positive control (100% RBCs cell lysis). The values are mean ± SD of triplicate samples (n = 3).

avoiding the commonly seen burst release of medications. Also,[50] evaluated the physicochemical properties of CMC and PVA films by cross-linking them with amino acids. The prepared sample showed promising antibacterial activity against *B. cereus* and *E. coli*. The L-histidine cross-linked CMC/PVA film is an appropriate antibacterial agent. The membrane fabricated the guar gum, polyvinyl alcohol and chitosan.[34] The change in concentrations of guar gum (GG) and chitosan has a promising impact on the swelling performance or permeability of these films. Membrane (B-2) of specific composition showed excellent swelling, permeability and absorption. The B-2 membrane showed promising activity against microorganisms. Cytotoxic analysis testing also revealed that the prepared membranes have potential for biomedical applications.

The fabrication of a CMC/PVA/dextrin-based polymeric membrane for the controlled release of cefixime with enhanced antibacterial activity represents a promising advancement in drug delivery systems. However, despite its potential, the study encounters several limitations that warrant consideration. Although the CMC/PVA/dextrin-based polymeric membrane for controlled drug delivery is thoroughly examined for its antibacterial activity and release kinetics, its scalability and repeatability during manufacture are not examined. Furthermore, the assessment of antimicrobial activity is predominantly conducted in controlled laboratory settings, which may constrain the generalizability of results in real-world contexts. By addressing these issues, the viability of the membrane for real-world uses could be better understood. Overall, the study shows promising results; however, in order to accurately assess the potential of the CMC/PVA/dextrin-based polymeric membrane for controlled drug delivery applications, these limitations must be addressed.

Conclusion

The CMC/PVA/dextrin was used to fabricate the hydrogel membrane by solvent casting method. These prepared membranes were characterized and their cefixime controlled release investigation revealed that the drug was released in 120 min in the phosphate-buffered saline (PBS) solution. The surface morphology and thermal stability of the prepared hydrogel membrane were changed

significantly between drug-loaded and unloaded membranes. The hydrogel biodegradation was studied at pH ~ 7.4, which was also affected due to drug loading in the membrane. The loaded membrane also showed promising antibacterial activity against a panel of microorganisms. In response to enhanced properties and controlled cefixime drug release. The findings conclude that the prepared hydrogels could be used for the controlled release of drugs for the treatment of infectious diseases.

Authors Contribution

Arif Nazir, Fadia Ameen, Dure Najaf Iqbal: Investigation: Roles/Writing – original draft; Conceptualization; Supervision; Methodology, Samiah H. Al-Mijalli, Mazhar Abbas: Project administration; Software; Resources Munawar Iqbal, Naveed Ahmad: Visualization; Data Curation; Writing – review & editing.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ORCID iDs

Arif Nazir https://orcid.org/0000-0002-9412-6100
Naveed Ahmad https://orcid.org/0000-0002-5847-903X
Munawar Iqbal https://orcid.org/0000-0001-7393-8065

Supplemental Material

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